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DREAMM-8: A Phase III Study of the Efficacy and Safety of Belantamab Mafodotin with Pomalidomide and Dexamethasone (BPd) vs Pomalidomide plus Bortezomib and Dexamethasone (PVd) in Patients with Relapsed/Refractory Multiple Myeloma (RRMM)

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Background

Aims:

To evaluate the efficacy and safety of belantamab mafodotin (belamaf, BLENREP) in combination with pomalidomide and dexamethasone (Pd) compared with Pd plus bortezomib (Pvd) in patients with RRMM

Unmet need

Patients with MM relapsed/refractory to immunomodulatory drugs and a PI have a poor prognosis (median OS of 15.2 months);¹ for those who are also refractory to daratumumab, OS is further reduced (median OS 8.6 months).² Novel, well-tolerated treatments that induce lasting responses are warranted¹⁻²

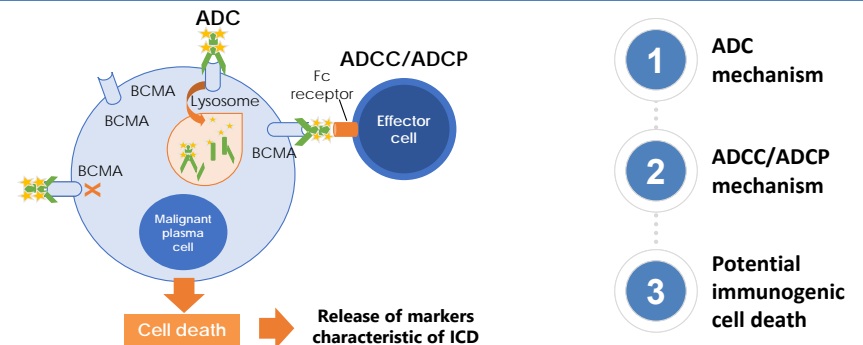
Combination regimens

- Pd is a standard of care treatment for patients with RRMM;³ however the median PFS achieved is only 4.2 months⁴ so it is generally used in a triplet regimen
- Pvd is an approved triplet regimen that has demonstrated improved anti-myeloma activity versus doublet regimens, such as Vd;⁵ there is a need for other triplet regimens containing immunomodulatory and/or novel agents⁶
- Pre-clinical data in animal models suggest significant added benefit (efficacy and survival) of belamaf combined with Pd over single agents⁷
- Preliminary data from an ongoing Phase I/II study (NCT03715478) evaluating BPd have shown manageable safety and promising clinical activity in patients with RRMM⁸

Belamaf

- First-in-class BCMA-targeting ADC with a multimodal mechanism of action^{9,10} approved in the US and the EU^{11,12}
- In the Phase II DREAMM-2 study, single-agent belamaf demonstrated deep and durable responses with a manageable safety profile in heavily pre-treated patients with RRMM¹³
- At 13 months of follow-up, responses with belamaf (2.5 mg/kg; IV* Q3W) were sustained; ORR was 32%; estimated median DoR and OS were 11.0 and 13.7 months, respectively.¹⁴ At the data cut-off, † 10% (10/97) of patients remained on study treatment

Belamaf Mechanisms of Action[†]



*Administered over 0.5–1hr as an outpatient; †Data cut: January 2020; ‡Image adapted from Richardson P, et al. Presented at the 61st Annual Meeting of the American Society of Hematology, December 7–10, 2019, Orlando, FL. Poster 1857.

ADC, antibody-drug conjugate; ADCC/P, antibody-dependent cellular cytotoxicity/phagocytosis; BCMA, B-cell maturation antigen; belamaf, belantamab mafodotin; BPd, belamaf plus pomalidomide and dexamethasone; DoR, duration of response; IV, intravenously; OS, overall survival; ORR, overall response; Q3W, every 3 weeks; Pd, pomalidomide and dexamethasone; Pvd, pomalidomide, bortezomib, and dexamethasone; RRMM, relapsed/refractory multiple myeloma; Vd, bortezomib and dexamethasone.

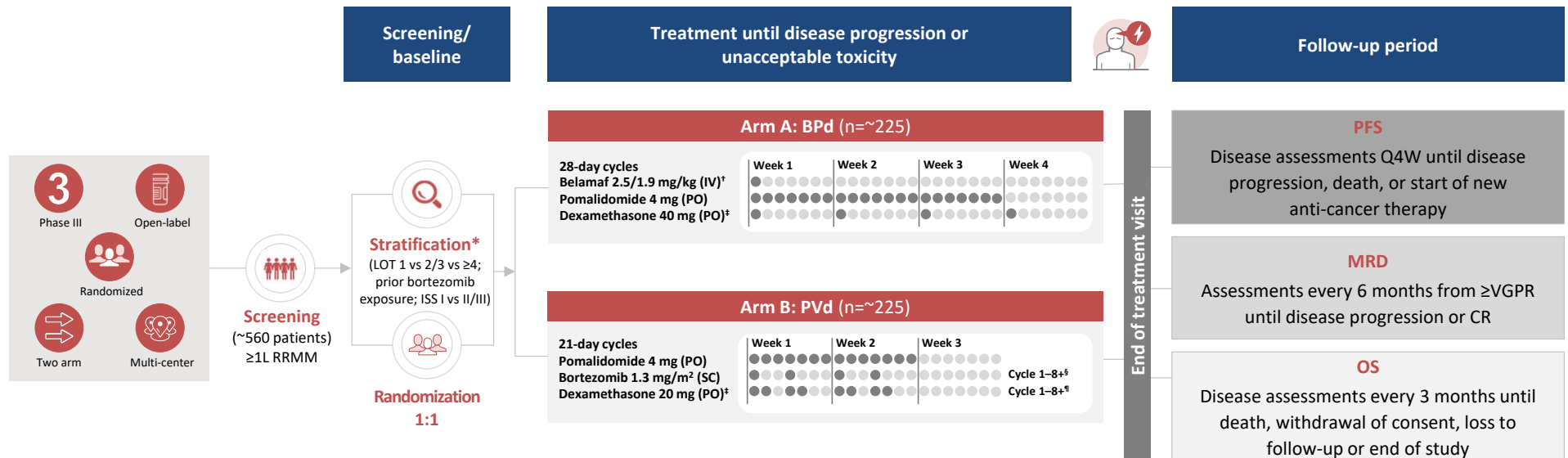
1. Kumar SK, et al. *Leukemia* 2017;31:2443; 2. Chai A, et al. *N Engl J Med* 2019;381:727–38; 3. Dimopoulos M, et al. *Leukemia* 2020; DOI:10.1038/s41375-020-01021-3; 4. Richardson P, et al. *Blood* 2014;123(12):1826; 5. Richardson P, et al. *Lancet Oncol* 2019;20:781; 6. Holstein S, et al. *Drugs* 2017;77:505; 7. Montes De Oca R, et al. AACR 2020. Available from: https://cancerres.aacrjournals.org/content/80/16_Supplement/6711 [accessed: 28 Oct 2020]; 8. Trudel S, et al. EHA 2019; Poster 294851; 9. Montes De Oca R, et al. EHA 2019; Poster PF558; 10. Tai YT, et al. *Blood* 2014;123:31288; 11. US Food and Drug Administration. BLENREP [Package Insert]. Available from: https://www.accessdata.fda.gov/drugsatfda_docs/label/2020/761158s000lbl.pdf [Accessed Oct 26, 2020]; 12. European Medicines Agency. BLENREP SmPC. 2020. Available from: <https://www.ema.europa.eu/en/medicines/human/EPAR/blenrep/blenrep-authorisation-details-section> [Accessed 26 Oct, 2020]; 13. Lonial S, et al. *Lancet Oncol* 2020;21:207; 14. Lonial S, et al. ASCO 2020 Poster 436.



Methods

The DREAMM-8 trial (NCT04484623) is a randomized, open-label, multi-center, Phase III study evaluating the efficacy and safety of BPd (Arm A) compared with Pvd (Arm B) in patients with RRMM. This is a registrational study

Study Design



*No more than 50% of patients with ≥2 prior lines of treatment and no more than 15% of patients with ≥4 prior lines; [†]Belamaf: 2.5 mg/kg in Cycle 1 and 1.9 mg/kg in Cycle 2+; [‡]Dexamethasone: dose may be reduced by half in patients >75 years of age or those with comorbidities or intolerant to dexamethasone; [§]Bortezomib: Cycles 9+ on Days 1 and 8; [¶]Dexamethasone: Cycles 9+ on Days 1, 2, 8, and 9. 1L, first line; ADA, anti-drug antibodies; belamaf, belantamab mafodotin; BPd, belamaf plus pomalidomide and dexamethasone; DoR, duration of response; IV, intravenously; ISS, International Staging System; LOT, line of treatment; OS, overall survival; PFS, progression-free survival; PO, orally; Pvd, pomalidomide, bortezomib, and dexamethasone; Q4W, every 4 weeks; RRMM, relapsed/refractory multiple myeloma; SC, subcutaneous.

Objectives and Endpoints

Primary

Objective

Compare the efficacy of BPd vs. PVd

Endpoint

PFS

Key Secondary

Objective

Further assess clinical activity of BPd vs. PVd

Endpoints

MRD negativity rate*

Secondary

Objective

- Further assess the efficacy of BPd
- Evaluate the safety and tolerability of BPd
- Describe exposure of belamaf when administered with Pd
- Evaluate the PK of BPd
- Assess ADAs against belamaf
- Evaluate the safety and tolerability of belamaf based on self-reported symptomatic AEs when administered with Pd
- Evaluate and compare changes in symptoms and HRQoL

Endpoints

- ORR, CRR, \geq VGPR rate, DoR, TTBR, TTR, TTP, OS, PFS2
- AEs and changes in laboratory parameters, ocular findings
- Plasma concentrations, total mAb, and cys-mcMMAF
- Derived PK parameter values
- Incidence and titers of ADAs
- Changes from baseline in symptoms and related impacts, as measured by PRO-CTCAE
- Change from baseline in HRQoL, as measured by EORTC QLQ-C30 and EORTC IL52

*Defined as percentage of patients who are MRD negative by next generation sequencing.

ADA, anti-drug antibody; AE, adverse event; belamaf, belantamab mafodotin; BPd, belamaf plus pomalidomide and dexamethasone; CRR, complete response rate; cys-mcMMAF, cysteine-maleimidocaproyl monomethyl auristatin F; DoR, duration of response; EORTC QLQ-C30 European Organization for Research and Treatment of Cancer Quality of Life Questionnaire; HRQoL, health related quality of life; mAb, monoclonal antibodies; MM, multiple myeloma; MRD, minimal residual disease; ORR, overall response rate; OS, overall survival; ORR, overall response rate; Pd, pomalidomide and dexamethasone; PFS, progression-free survival; PFS2, PFS after initiation of new anticancer therapy; PK, pharmacokinetics; PRO-CTCAE, Common Terminology Criteria for Adverse Events (CTCAE) & Patient Reported Outcomes-CTCAE; PVd, pomalidomide plus bortezomib and dexamethasone; TTBR, time to best response; TTP, time to progression; TTR, time to response; VGPR, very good partial response.



Patient Population



Key inclusion criteria

- Age ≥ 18 years
- Confirmed MM (IMWG criteria)¹
- Measurable disease (according to serum and/or urine M-protein and/or serum free light chain levels)
- ECOG Performance Status 0–2
- ≥ 1 prior line of therapy,* including a lenalidomide-containing regimen[†]
- History of autologous SCT (if >100 days prior to initiation of study treatment and no active infections)
- All prior treatment-related toxicities Grade ≤ 1 at the time of enrolment[‡]
- Acceptable organ system function
- Informed consent



Key exclusion criteria

- Active plasma cell leukemia, symptomatic amyloidosis or active POEMS syndrome
- Prior allogeneic SCT
- Prior exposure to anti-BCMA therapy
- Prior treatment with or intolerance to pomalidomide, or intolerance/refractory to bortezomib
- Prior treatment with other mAbs within 30 days, investigational agent or systemic anti-myeloma therapy within 14 days or 5 half-lives (whichever is shorter), plasmapheresis within 7 days of first dose of study drug
- Evidence of cardiovascular risk
- Presence of active renal condition, mucosal or internal bleeding, cirrhosis or current unstable liver or biliary disease, infection or HIV
- Ongoing Grade ≥ 2 peripheral neuropathy or neuropathic pain
- Current corneal epithelial disease (except mild punctate keratopathy)

*Patients must have documented disease progression during or after the most recent therapy; [†]Lenalidomide must have been administered for ≥ 2 consecutive cycles; [‡]Except alopecia.

BCMA, B-cell maturation antigen; ECOG, Eastern Cooperative Oncology Group Performance Status; HIV, human immunodeficiency virus; IMWG, The International Myeloma Working Group; mAb monoclonal antibody; MM, multiple myeloma; POEMS, polyneuropathy, organomegaly, endocrinopathy, monoclonal plasma proliferative disorder, and skin changes; SCT, stem cell transplantation.

1. Kumar S, et al. *Lancet Oncol* 2016;17:e328–46.



Current status

The DREAMM-8 study started in October 2020 and aims to enroll 450 patients with RRMM worldwide

Estimated Study Dates



Primary Completion

~ April 2022

Study End

~ January 2027



Currently participating countries



Australia



Greece



Spain



United States of America

More countries will be added soon

The BCMA-targeting MoA of belamaf supports combination with other therapies, including Pd, offering the potential for a manageable safety profile with enhanced efficacy

Phase I data on Bpd are presented as an oral presentation 725 at this meeting. Belamaf is being evaluated in other combination strategies in various MM settings (posters 1419, 2302, 3247). Further analyses of the pivotal DREAMM-2 study of single-agent belamaf are presented at this meeting (posters 1417, 2278, 3221, 3224, 3248)

BCMA, B-cell maturation antigen; belamaf; belantamab mafodotin; Bpd, belamaf plus pomalidomide and dexamethasone; MM, multiple myeloma; MoA, mode of action; Pd, pomalidomide and dexamethasone; RRMM, relapsed/refractory multiple myeloma National Institutes of Health. ClinicalTrials.gov. 2020. Available from: <https://clinicaltrials.gov/ct2/show/NCT04484623>. [Accessed Oct 14, 2020].



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